Effectiveness of nimodipine on non-traumatic subarachnoid hemorrhage based on computed tomography angiography

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ABSTRACT: In this study, we aimed to investigate the effectiveness of nimodipine on cerebral vasospasm in patients with SAH by evaluating their blood pressure and the GCS. This retrospective study was performed at the Department of Neurology, Soetomo Teaching Hospital, Surabaya. The study participants were those who had been diagnosed with non-traumatic subarachnoid hemorrhage and received nimodipine between January and December 2015. The results indicated that more than 70% of patients received 60 mg oral nimodipine per day for more than 21 days. The calcium antagonist decreased the proportion of patients with poor outcomes and ischemic neurological deficits after aneurysmal subarachnoid hemorrhage. The risk of rebleeding from an aneurysm was more than 5% in the first 24 h, which gradually decreased over time. There were no significant changes in the GCS and blood pressure between patients with SAH who received nimodipine therapy. However, changes in the GCS and blood pressure were observed during the administration of nimodipine.

1 INTRODUCTION

According to the World Health Organization (WHO), stroke is a brain functional disorder that occurs suddenly with clinical signs and symptoms, both focal and global, lasting more than 24 h, or directly causing death due to circulatory brain disorders (WHO 2010). Stroke occurs due to decreased blood supply to the brain resulting from blockage or rupture of blood vessels to the brain (Ginsberg 2008). According to the American Stroke Association, stroke is the third major factor contributing to the world's mortality rate after heart disease and cancer, with prevalence rate of 2,980,000 people and morbidity of 50,000 people every year. Approximately 795,000 people in the United States experience stroke every year, leading to more than 134,000 deaths (Goldstein et al. 2008). A total of 4 million Americans have a stroke-neurological deficit. Two-thirds of this deficit is moderate to severe. On the basis of a report in 2011, an incidence of stroke occurs almost every 45 s and a person dies due to stroke every 4 s. In addition, stroke also has a high rate of morbidity in causing disability (Irdelia 2014).

On the basis of data from the 10 most prevalent diseases in Indonesia in 2013 and on the basis of the diagnosis of health workers, the prevalence of stroke in Indonesia is 7.0 per mile and people diagnosed with stroke symptoms are 12.1 per mile. The highest prevalence of stroke was found in North Sulawesi Province (10.8%) and the lowest in Papua (2.3%), while it was 7.7% in Central Java (Ministry of Health 2013). According to the Central Java Provincial Health Office (2012), stroke can be divided into hemorrhagic stroke and non-hemorrhagic stroke. The prevalence of hemorrhagic stroke in Central Java in 2012 was 0.07 higher than that in 2011 (0.03%). The highest prevalence in 2012 (1.84%) was found in Kudus Regency. The prevalence of non-hemorrhagic stroke in 2012 was 0.07% lower than that in 2011 (0.09%). It is estimated that 87% of patients with stroke have ischemic stroke and 13% have stroke bleeding. In bleeding strokes, 10–20% is intracerebral hemorrhage and 3% is subarachnoid hemorrhage (Gofir 2009). Subarachnoid hemorrhage (SAH) is relatively small in number (<0.01% of the population in the United States), while it is 4% and 4.2% in ASEAN and Indonesia, respectively. Nevertheless, the mortality and morbidity rates are very high, reaching up to 80% (Misbach 2011, Dalbjerg et al. 2012).

There are two common types of strokes, namely ischemic and hemorrhagic strokes. Ischemic stroke occurs when the flow in a vessel is disturbed by atherosclerotic plaques where thrombus is formed. Thrombus can also form elsewhere, such as in the atria in patients with atrial fibrillation and enter

the brain as an embolus, causing cerebral infestation. Hemorrhagic stroke is due to ruptured intracerebral blood vessels, resulting in bleeding into the subarachnoid space or directly into the brain tissue. Some of the vascular lesions that can cause subarachnoid hemorrhage (SAH) are saccular aneurysms (Berry) and arteriovenous malformations (MAV) (Ganong 2008). Subarachnoid hemorrhage is one of the neurological emergencies caused by the rupture of the blood vessels in the subarachnoid space (Setyopranoto 2012). In non-traumatic cases, 80% are due to the outbreak of a saccular aneurysm. Saccular aneurysms are a process of acquired vascular degeneration as a result of the process of hemodynamics in the bifurcation arteries of the brain, especially in the "Circle of Willis", often in anterior common artery, medial cerebral artery, anterior cerebral artery, and posterior common artery. Cerebral vasospasm is a chronic narrowing of the cerebral arteries, sometimes severe, but reversible, which comes days after SAH. Risk of vasospasm depends on the thickness of the blood in the subarachnoid and ventricle caused by the rupture of the saccular aneurysm, vascular malformation, or brain tumors, which experience significant bleeding in the subarachnoid space at the cerebral base (Dalbjerg et al. 2012). According to the 2011 Stroke Guidelines, therapeutic treatment of SAH grade I or II, according to Hunt and Hess (H & H), is to identify and overcome the headache as soon as possible, and in patients with SAH stage III, IV, or V who show signs of intracranial high pressure, intensive care is required. Surgical procedures are also performed to reduce the risk of rebleeding, that is, clipping or endovascular coiling after aneurysm rupture in SAH (Connolly et al. 2012). The recommendation for SAH treatment is neurointensive management therapy and prevention of complications, especially in patients with critical illnesses, such as epilepsy, infection, previous bleeding, and delayed cerebral ischemia (Dipiro 2011). In delayed cerebral ischemia, therapy for PS stroke prevention is nimodipine. Nimodipine is a class of calcium channel blockers that can reduce the severity of neurological function due to vasospasm (Setyopranoto 2012). Use of nimodipine has been approved by the FDA for the prevention and treatment of cerebral vasospasm (Keyrouz 2007). According to the 2011 Stroke Guidelines, the treatment of cerebral vasospasm begins with the treatment of ruptured aneurysms, maintaining a normal circulatory blood volume (euvolemia) and avoiding hypovolemia.

Various studies have been conducted to determine the effectiveness of nimodipine drugs in SAH patients. From the 2009 Harsono study, nimodipine is a drug that can pass through the blood–brain barrier and inhibit calcium ions into cells by reducing the contractile state of smooth muscle at depolarization and causing vasoconstriction. The use of nimodipine in vasospasm patients after SAH aneurysms has proved to improve neurological recovery and reduce cerebral infestation. Vergouwen et al. (2006) conducted a randomized study of 1,074 patients with non-traumatic subarachnoid hemorrhage using oral nimodipine compared with placebo to determine the effectiveness of oral nimodipine in reducing cerebral infarction and therapy outcome after subarachnoid hemorrhage.

Nimodipine was administered every 4 h within 96 h of SAH aneurysm and was given for 21 days in 278 patients, whereas 276 patients received placebo. At the end of 21 days, 33% and 22% of patients had completely recovered from ischemic neurologic deficits in the nimodipine group and the placebo group, respectively. Severe neurologic deficits in arterial SAH patients with arterial vasospasm were significantly more common in the placebo group (Harsono 2009). According to the American Nimodipine Study Group of Patients, the use of nimodipine within 18 h after the onset of stroke in America has resulted in a positive increase in therapy outcome. Treatment with the use of nimodipine between 12 and 24 h showed no effect, whereas use at 24 h after SAH showed poor outcome (Horn et al. 2001). Clinical trials were conducted on 12 children with an average age of 11.8 ± 3.3 years up to 3.5–17.3 years of age who had been diagnosed with non-traumatic PSA with oral administration of nimodipine 1 mg/kg every 4 h. The results of this study indicated that nimodipine therapy produced varied results. Vasospasm was observed in 67%, new infarction 33%, recurrent bleeding and hypotension in 17%. However, clinical profile data in patients showed positive outcome, that is, minor neurological and cognitive function deficits in two-thirds and absent in the remaining one-third (Heffren 2015). In other clinical trials, where intra-arterial administration of nimodipine was provided in 29 patients diagnosed with cerebral vasospasm from SAH in Japan between 2009 and 2011, there was a statistically significant increase in blood vessel diameter and clinical symptoms in the cerebral angiography profile. The percentage increase in vascular diameter was more than 40% in eight patients, 30–40% in one patient, 20–30% in eight patients, 10–20% in eight patients, and less than 10% in four patients (Kim et al. 2012). A retrospective study was conducted at Aga Khan University Hospital to determine the occurrence of vasospasm, site of intracranial aneurysm, and size of aneurysm by looking at the angiography profile of patients with SAH. The study was performed using digital subtraction angiography (DSA).

In patients with SAH stroke in Indonesia, oral nimodipine is often used to correct neurological deficits caused by vasospasm (Perdossi 2011). From a clinical trial study, it was found that nimodipine may improve neurologic function and prevent cerebral vasospasm in patients with SAH stroke (Gijn 2001). Another study mentioned that nimodipine is safe to use in patients with PSA stroke. However, results of the study based on clinical outcome need to be taken further to get a better overall profile in patients with non-traumatic PSA stroke (Heffren 2015). On the basis of the above information, we conducted a study on the use of nimodipine in a number of non-traumatic subarachnoid stroke bleeding patients at Dr. Soetomo Hospital to determine the therapeutic effectiveness of the patients' cerebral angiography profile, including the dose of drug administration, the frequency of administration, the duration of therapy, and the side effects of the drug (ESO). The study was conducted in a retrospective manner and focused on the effectiveness on the use of nimodipine in order to improve the quality of life of patients with non-traumatic subarachnoid stroke bleeding.

2 METHODS

2.1 *Study design*

This study was a retrospective study wherein treatment was not given to the studied patients, and observed data were the patients' development in the past. Data obtained were analyzed descriptively, because this study aims to describe the pattern of nimodipine use in patients with non-traumatic subarachnoid hemorrhage at the inpatient ward of Department of Neurology, Dr. Soetomo Teaching Hospital, Surabaya.

2.2 *Study subjects*

The subjects of this study were patients who had a non-traumatic subarachnoid hemorrhage stroke treated at the inpatient ward of Department of Neurology, Dr. Soetomo Teaching Hospital between January and December 2015 who met the inclusion criteria. The inclusion criteria were inpatients with head CT scan, CT angiography/cerebral angiography, and a diagnosis of non-traumatic subarachnoid hemorrhage stroke. Patients with non-traumatic subarachnoid hemorrhage stroke were given nimodipine therapy.

3 RESULTS AND DISCUSSION

In this study, we aimed to determine the use of nimodipine in patients with non-traumatic subarachnoid hemorrhage stroke based on angiography. The study was conducted retrospectively by retrieving data from the medical records of the patients from January to December 2015 held in the Central Medical Record Room. Medical records referred to were those from the inpatient ward of the Department of Neurology, Dr. Soetomo Teaching Hospital, Surabaya. The total sample size was 59 patients, out of which 19 patients fulfilled the inclusion criteria with a final diagnosis of subarachnoid hemorrhage with CT scan/CT angiography and who had taken nimodipine during treatment at Neurology Inpatient Ward, Dr. Soetomo Hospital, Surabaya.

3.1 *Patients' demographic data*

Prevalence of non-traumatic SAH stroke at Dr. Soetomo Hospital, Surabaya by sex shows that females were more commonly affected than males (14 persons (74%) vs. 5 persons (26%)). The prevalence of non-traumatic SAH can be seen in Table 1.

Age distribution of patients with SAH who were treated at the inpatient ward, Department of Neurology, Dr. Soetomo Teaching Hospital, Surabaya, varied from 31 to 73 years. Of the 19 patients who met the inclusion criteria in this study, the largest number of patients (i.e., 11 patients (58%)) was in the age range 40–60 years. The age distribution of the patients' samples studied is presented in Table 2.

According to Table 1, patients with SAH were predominantly females, as many as 14 patients (74%), compared with males (5 patients (26%)). According to the Stroke Association 2013, the prevalence of stroke in 2010 in women was 80%, far higher than the 20% in men. This is due to genetic

Table 1. Sex distribution of patients meeting the inclusion criteria at Dr. Soetomo Teaching Hospital, Surabaya, between January and December 2015.

Sex	No. of patients	Percentage
Male	5	26
Female	14	74
Total	19	100

Table 2. Age distribution of patients meeting the inclusion criteria at the inpatient ward.

Age (years)	No. of patients	Percentage
<40	2	11
40–60	11	58
≥60	6	32
Total	19	100

factors as well as the risk factor for the use of oral contraceptives for long periods by the female sex, although confirmation from further studies is needed (Gijn et al. 2001). The age of patients with SAH who participated in the study also varied greatly in the range of 31–73 years. Table 2 shows that most patients (i.e., 11 patients (58%)) were in the age group of 40–60 years. Of the 19 patients, 2 (11%) were in the age group of <40 years, 11 (58%) in the age group of 40–60 years, and 6 (32%) in the age group of >60 years. This is consistent with the literature, which states that the majority of patients with SAH have an aneurysm, that is, in the age group of ≥30 years (Connolly et al. 2012).

3.2 *Previous history of disease and comorbidities*

The previous history and comorbidity of disease of the patients in this study includes diabetes mellitus, uncontrolled hypertension, stroke, and no disease history. The results indicated that of a total of 19 patients, the majority (i.e., 11 patients (58%)) had a history of hypertension (Table 3).

Hypertension itself is a major risk factor for SAH stroke, because increased blood pressure may weaken small arteries in the cranium and result in the artery losing its elasticity and becoming susceptible to cracking and brittle. The risk of stroke increases 1.6 times per 10 mmHg increase in systolic blood pressure and about 50% of stroke events can be prevented by blood pressure control (Indiana Stroke Prevention Task Force January 2006). The history of previous diseases in six patients (32%) was unknown, which is consistent with the literature that states genetic factors and a history of aneurysms in more than two family members (Thompson et al. 2015). In patients with SAH stroke, the most common comorbidities and other diagnoses of the disease during hospitalized treatment was hypertension in 10 out of the 19 patients. A total of 6 out of the 19 patients had aneurysmal disease 4 had dyslipidemia, 4 had hypokalemia, 2 had pneumonia, 1 had hydrocephalus, and 2 patients had no coexisting disease (Table 4).

Table 3. Medical history of patients receiving nimodipine therapy at the inpatient ward.

Disease history	No. of patients	Percentage
Diabetes mellitus	2	11
Hypertension	11	58
Stroke	1	5
No history	6	32
Total	19	100

Note: Patients may have more than one history of disease.

Table 4. Comorbidities in patients at the inpatient ward.

Comorbidity	No. of patients	Percentage
Hypertension	10	37
Aneurism	6	22
Dyslipidemia	4	15
Hypokalemia	4	15
Pneumonia	2	7
Hydrocephalus	1	4
Total	27	100

Note: Patients may have more than one history of disease.

Table 5. Surgical procedures performed in patients with SAH at the inpatient ward.

Surgical procedure	No. of patients	Percentage
Clipping	1	5
Coiling	9	47
VP shunt	2	11
No surgery	7	37
Total	19	100

3.3 *Surgery*

Surgical procedures performed on the patients were clipping, coiling, and VP shunt surgery, and a number of patients were not operated. The prevalence of operated patients can be seen in Table 5, which also shows the surgical procedures that have been performed on SAH patients. The results showed that out of the total 19 patients, 12 had underwent surgery, 9 patients (47%) had coiling operations, 2 (11%) had VP shunt surgery, and 1 patient (5%) had clipping operations. Coiling surgery is generally recommended as the first choice for handling brain aneurysms, as it is considered safer and more comfortable for patients (Bederson et al. 2009).

3.4 *Profile of nimodipine use*

Table 6 shows that the length of patient care at most is ≥21 days, that is, in 11 patients (58%). Five patients received treatment for 10–21 days (26%), and three patients <10 days (16%). The length of treatment of patients with SAH stroke was determined on the basis of the patient's level of consciousness (GCS), other complications of the disease, and the risk factors present in the patient (Misbach 2011).

In patients with non-traumatic subarachnoid hemorrhage, nimodipine was administered throughout hospital care through intervention and oral routes. There are, however, patients receiving alternate oral or per-oral intervention routes

Table 6. Duration of hospitalization at the inpatient ward.

Duration of hospitalization (days)	No. of patients	Percentage
<10	3	16
10–21	5	26
≥21	11	58
Total	19	100

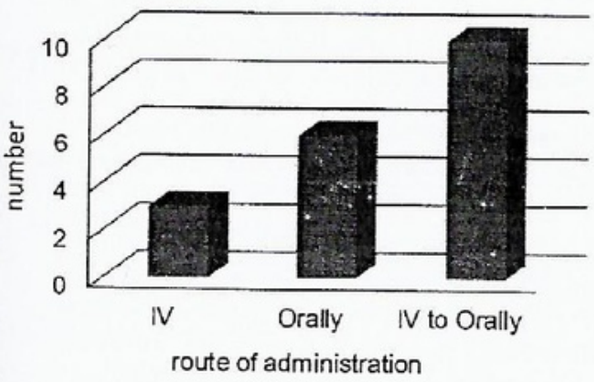

Figure 1. Routes of nimodipine administration at the inpatient ward, Department of Neurology, Dr. Soetomo Teaching Hospital, from January to December 2015.

(Figure 1). Nimodipine dose regimens administered to PSA patients per day were 60 mg and 50 ml.

The nimodipine dosage regimen administered to patients per day was 60 mg every 6 h per oral or a dose of 1–2 mg/h intravenously for 21 days (Perdossi 2011). According to the literature, the optimum dose of nimodipine for patients with SAH was 3600 mg per day for 3 weeks (Heffren et al. 2015). Nimodipine can be given six times a day because it has a short half-life, which is 2 h, so an additional dose can be taken every 4 h (Harsono 2009). It can be seen from Table 7 that the dose of nimodipine per day received by the patients in Dr. Soetomo Teaching Hospital was 4 × 60 mg in two patients (10%), 5 × 60 mg in one patient (16%), and 6 × 60 mg in three patients. It was found that as many as 70% of patient with SAH had received nimodipine therapy with oral route. The 2011 Stroke Guideline states that nimodipine should start with a dose of 1–2 mg/h IV on day 3 or orally 60 mg every 6 h for 21 days. The Heffren study (2015) suggests that administration of nimodipine should start with a dose of 6 × 60 mg for 3 weeks. From medical records, the significance or influence of low or high doses on the outcome of patients with SAH stroke cannot be observed. Therefore, further studies are still needed.

Table 7. Dosage regimens of nimodipine in patients at the inpatient ward.

Drug	Frequency	No. of patients	Percentage
Nimodipine Oral administration	4 × 60 mg	2	11
	5 × 60 mg	3	16
	6 × 60 mg	3	16
Nimodipine Intravenous administration	10 mg/50 ml/day	2	11
	12 mg/60 ml/day	1	1
Intravenous to oral administration		6	32
Oral to intravenous administration		2	11
Total		19	100

Table 7 shows that, out of 10 patients given nimodipine, 8 patients had a change of route of administration, 1 had changed dose, and 1 patient ended with the initial dose and underwent a change of route or dose during treatment. In the patient with medical record no. 12388xxx, nimodipine route was changed from IV to oral on day 3 for 3 days and dose was reduced to 6 × 60 mg on day 5, 4 × 60 mg on day 8, and 3 × 60 mg on day 13. Finally, on day 19, the dose was 2 × 60 mg. In the patient with medical record no. 12390xxx, the dose of nimodipine was reduced from 6 × 60 mg to 4 × 60 mg when the patient's condition improved. In the patient with medical record no. 12392xxx, the route was changed from oral to IV on day 19 when the patient's GSC worsened. Four patients had their route changed from IV to oral after an improvement in GSC conditions. No literature study states that the doses of nimodipine can be tapered off, but medical record data show one patient undergoing tapering off who did not follow the guideline. In addition to route changes, there was dose change from the initial dose at hospital admission adjusted to the patient's condition, especially their neurological condition. Increased doses occur when neurological condition of the patient does not progress with the initial dose. Therefore, the clinician may increase the dose of the nimodipine or change the route of administration to achieve improved patient neurological conditions.

3.5 *Angiographic data of patients in the positive and negative vasospasm groups*

In this study, angiography examination was performed to determine the presence of cerebral vasospasm and surgery was performed for the treatment of ruptured aneurysms to prevent the

occurrence of vasospasm. The profile of vasospasm was observed using cerebral DSA to determine the morphology and location of the aneurysm. Cerebral vasospasm is a major complication, continuation of which may result in death and disability in the SAH. Vasospasm occurred on days 3 and 4 after bleeding, peaking after 1 week and generally resolved after 2 or 3 weeks (Archavlis et al. 2013). Patients with non-traumatic SAH stroke underwent cerebral angiography to identify vasospasm. Out of a total of 59 SAH patients, 19 patients met the inclusion criteria.

In this study, treatment outcomes for the use of nimodipine were observed based on neurological conditions (GCS) and controlled blood pressure. In general, the neurologic conditions of the samples receiving nimodipine therapy improved. However, after being analyzed statistically, no difference was found in the outcome. The result of normality test at systole blood pressure during admission and discharge using the Kolmogorov–Smirnov test showed significance values of 0.934 and 0.367 ($\alpha > 0.05$). This indicates that the data in this study are normally distributed and, therefore, parametric analysis was used. Paired t-test was used to see if there was any difference in the nimodipine therapy regarding the patient's systolic blood pressure, and it was found that the p value was 0.068 ($\alpha > 0,05$). This suggests that there was no significant difference in systolic blood pressure during admission and discharge among patients receiving nimodipine therapy.

The effectiveness of the use of nimodipine based on the GCS at the time of admission and discharge in the study samples was tested by Wilcoxon's signed-rank test to observe the difference of therapy outcome to patients with non-traumatic SAH. It was found that the resulting p value was 0.307, which was higher than 0.05, indicating that there was no significant difference from nimodipine therapy. This means that there was no difference in the GCS during admission and discharge on nimodipine therapy outcome.

Table 8 shows that of the total patients, 11 showed positive vasospasm and 8 showed negative vasospasm. Of the 11 patients who showed positive vasospasm, 8 had improved, 1 died of complications, and 2 had an early discharge from the hospital. Of the 8 patients who improved, 2 had been receiving nimodipine therapy for 15 days and 6 patients had received therapy ≥21 days and had improved. According to the literature, nimodipine therapy begins at the beginning of SAH and continued for 21 days so as to prevent vasospasm and delayed cerebral ischemic (Harsono 2009).

The patients' condition during discharge can be seen in Table 9. The condition was found to be

Table 8. Angiographic profile of patients with SAH at the inpatient ward.

No. of patients	Duration of nimodipine administration (days)	Vasospasm	Outcome
6	17.3	Negative	Improved
2	17.5	Negative	No change
8	19.9	Positive	Improved
3	4.7	Positive	No change

Table 9. Patients' condition during discharge from the inpatient ward.

Patients' condition during discharge	No. of patients	Percentage
Improved	14	74
No change	3	16
Death	2	10
Total	19	100

improved (discharged) in 14 patients (74%), no change (early discharge) in 3 patients (16%), and death in 2 patients (11%; Table 9). Patients died due to complications from the worsening of the disease, such as increased intracranial pressure, which, in turn, causes herniation, hydrocephalus, and unidentifiable cases. From the results of the study conducted at the inpatient ward, Dr. Soetomo Teaching Hospital, it was found that patients who had been diagnosed with SAH stroke started with nimodipine therapy early in the diagnosis to reduce the risk of ischemic complications and as a prophylaxis of cerebral vasospasm. Nimodipine has a working mechanism by inhibiting the transfer of calcium ions into the cells and thus inhibiting smooth muscle contraction of blood vessels (Harsono 2009). The effects of inhibition of smooth muscle contraction can reduce the outcome of poor and delayed cerebral ischemic due to vasospasm (Herzfeld 2014).

The evaluation was performed by assessing the achievement of blood pressure target of patients with non-traumatic SAH stroke with nimodipine therapy. Recommended blood pressure target based on JNC 8 year 2014 for PSA patients is systolic blood pressure <140 mmHg or diastolic pressure <90 mmHg. In this study, the patient's blood pressure was measured on a daily basis to determine the achievement of blood pressure target from the use of nimodipine. The differential effect of nimodipine therapy on the patient's systolic blood pressure analyzed through paired t-test resulted in a p value of 0.068, higher than alpha at 0.05, indicating no significant difference in systolic blood pressure during admission and

discharge in patients receiving nimodipine therapy. Glasgow Coma Scale (GSC) is a clinically used and semi-quantitative scale of consciousness, based on eye opening, verbal, and motor responses. In patients with SAH stroke receiving nimodipine therapy, GSC monitoring is essential to identify GSC changes after receiving nimodipine therapy and other therapies. GSC examination is indispensable for monitoring ICT change (Barker 2002). From the data obtained by the analysis, the effectiveness of nimodipine use was measured on the basis of the GCS during admission and discharge from the hospital. From the results of Wilcoxon's signed-rank test showing differences in the outcome of therapy for non-traumatic SAH patients, it can be seen that p value produced was 0.307, higher than 0.05, indicating that there was no significant difference from nimodipine therapy. This means that there is no difference in the GCS between admission and discharge toward the outcome of nimodipine therapy.

There are some limitations to this study because of incomplete recordings in patients' records, such as patients' clinical data (blood pressure and GCS) and duration of nimodipine therapy. This results in less than optimal monitoring of the effectiveness of blood pressure and GSC in the patients. Side effects caused by nimodipine, such as decreased blood pressure (hypotension), impaired liver function, edema, headache, gastrointestinal complaints, muscle pain, diarrhea, rash, and tachycardia, were not found in the patients, based on medical record-keeping data. Drug interactions may occur in the use of nimodipine with rifampicin, phenobarbital, phenytoin, or carbamazepine on CYP3 A4 cytochrome isoenzymes that alter nimodipine clearance. However, in this study, no review was done of drug-related problems in the patients.

4 CONCLUSIONS

This study showed that the administration of nimodipine did not reduce the systemic blood pressure in patients with non-traumatic SAH. Furthermore, despite receiving nimodipine therapy from day 1, vasospasm was still present in the majority of the patients. The use of nimodipine in non-traumatic SAH stroke therapy was consistent with the guidelines.

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